EXHIBIT D

US006399365B2

(12) **United States Patent**
Besemer et al.

(10) **Patent No.: US 6,399,365 B2**
(45) **Date of Patent: Jun. 4, 2002**

(54) **BIOARRAY CHIP REACTION APPARATUS AND ITS MANUFACTURE**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/907,196**

(22) Filed: **Jul. 17, 2001**

Related U.S. Application Data

(63) Continuation of application No. 09/302,052, filed on Apr. 29, 1999, now Pat. No. 6,287,850, which is a continuation of application No. 08/485,452, filed on Jun. 7, 1995, now Pat. No. 5,945,334, which is a continuation-in-part of application No. 08/255,682, filed on Jun. 8, 1994, now abandoned.

(51) Int. Cl.[7] C12G 1/08; C12M 1/34; C12P 19/34; C07H 21/02; C07H 21/04

(52) U.S. Cl. **435/287.2**; 435/6; 435/7.1; 435/91.1; 435/91.2; 435/285.1; 536/22.1; 536/23.1; 536/24.3; 536/24.31; 536/24.32; 536/24.33

(58) Field of Search 435/6, 7.1, 91.1, 435/91.2, 285.1, 287.2; 536/22.1, 23.1, 24.3, 24.31, 24.32, 24.33

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Primary Examiner—Jeffrey Siew
(74) *Attorney, Agent, or Firm*—Philip L. McGarrigle; Alan B. Sherr; Ivan D. Zitkovsky

(57) **ABSTRACT**

A package for hybridization includes a substrate and a housing. The substrate has a first surface that includes an array of probes having biological polymers immobilized thereon. The housing includes a fluid cavity constructed and arranged for hybridization of a target to a probe of the probe array located inside the fluid cavity. The housing also includes a bar code.

58 Claims, 46 Drawing Sheets

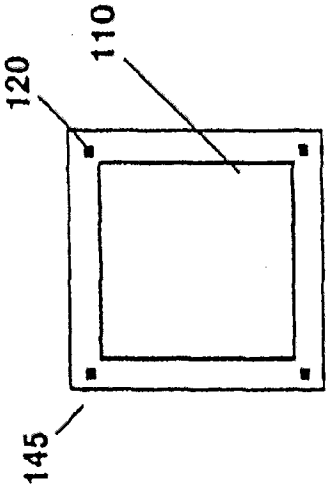


FIG. 1B

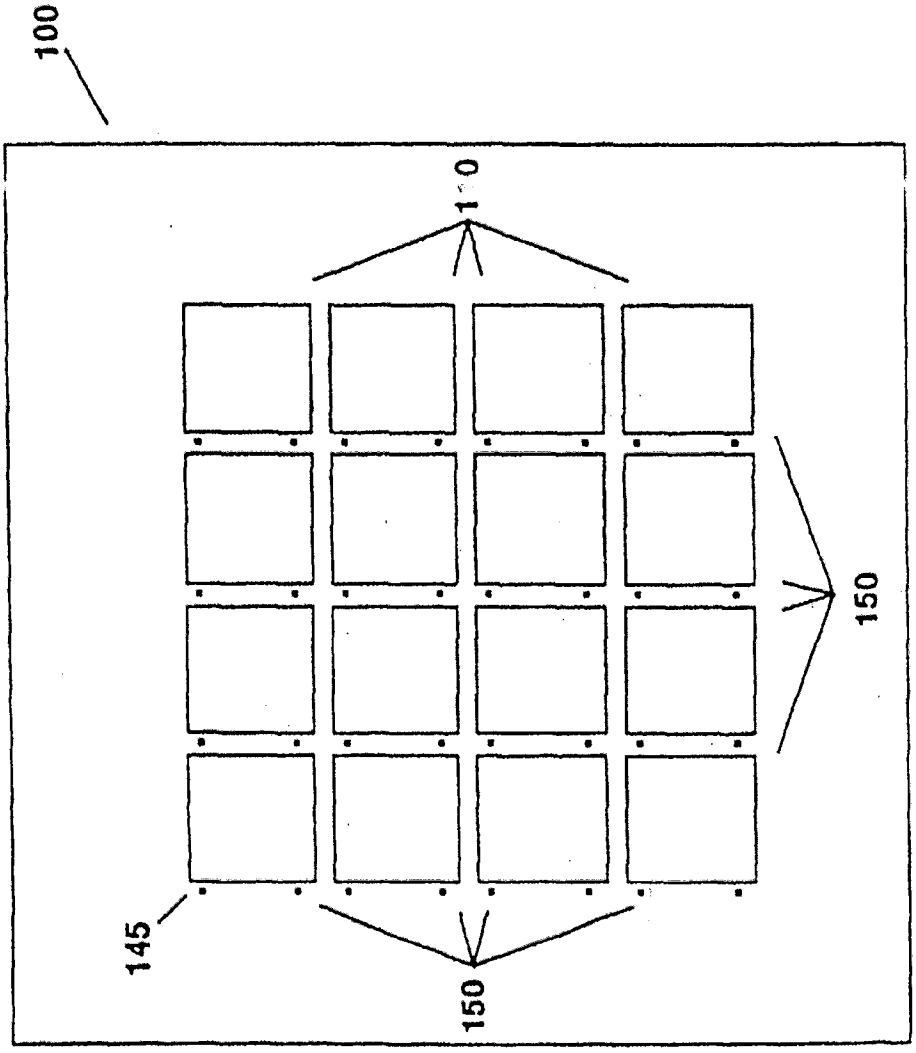


FIG. 1A

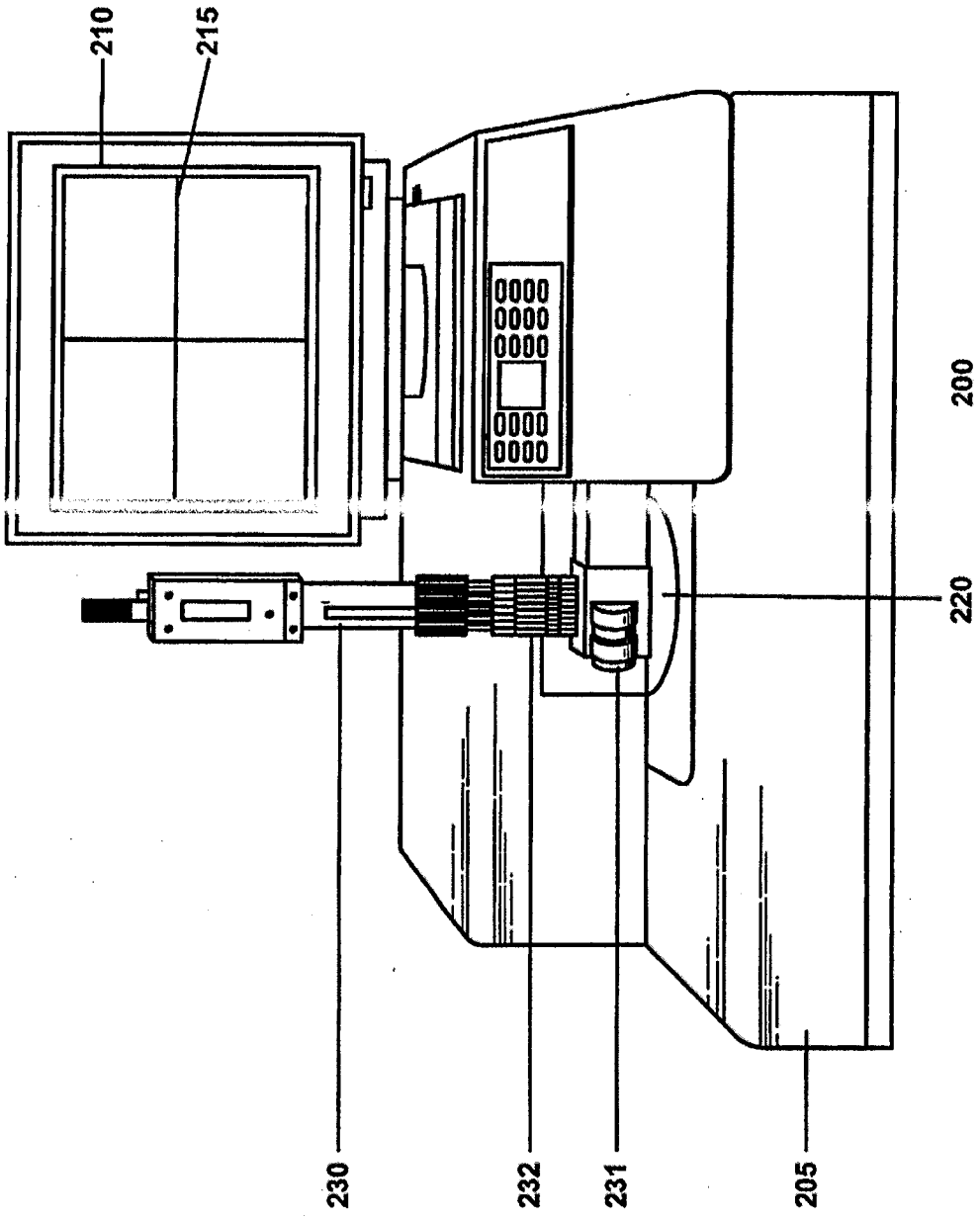


FIG. 2A

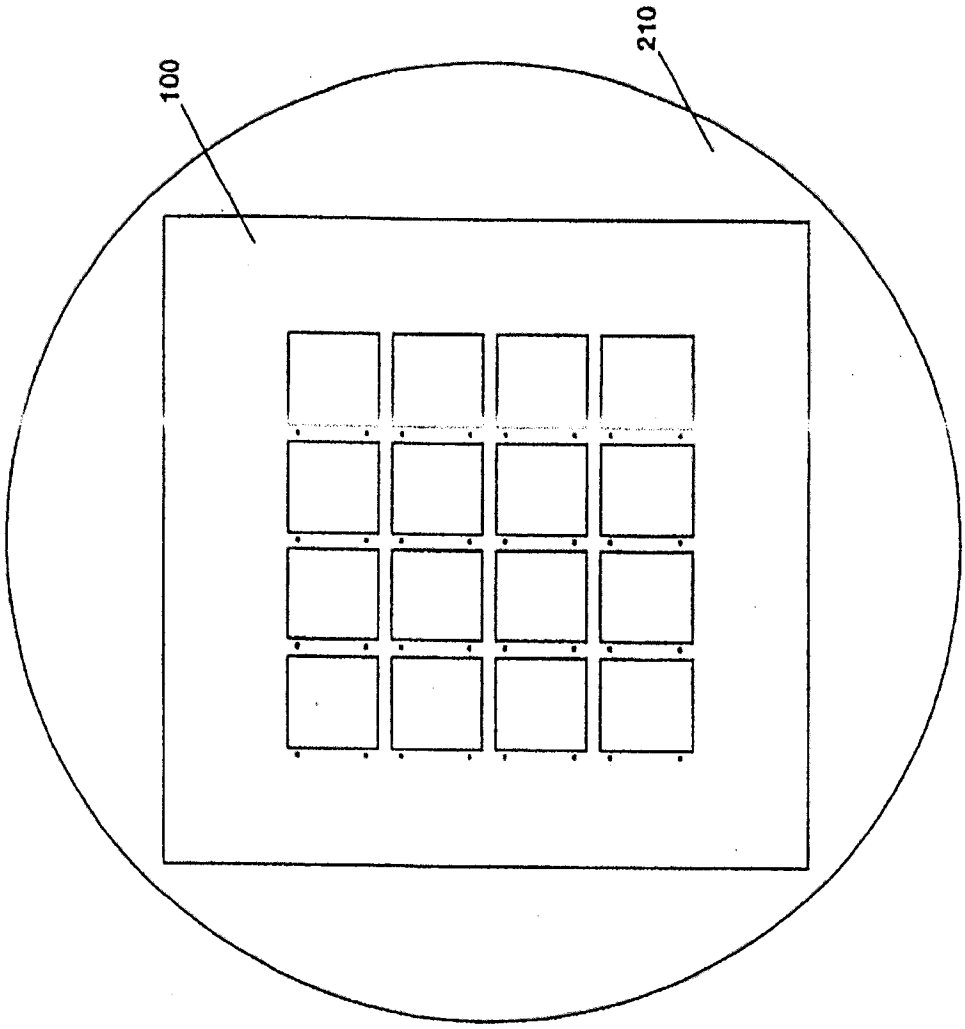


FIG. 2B

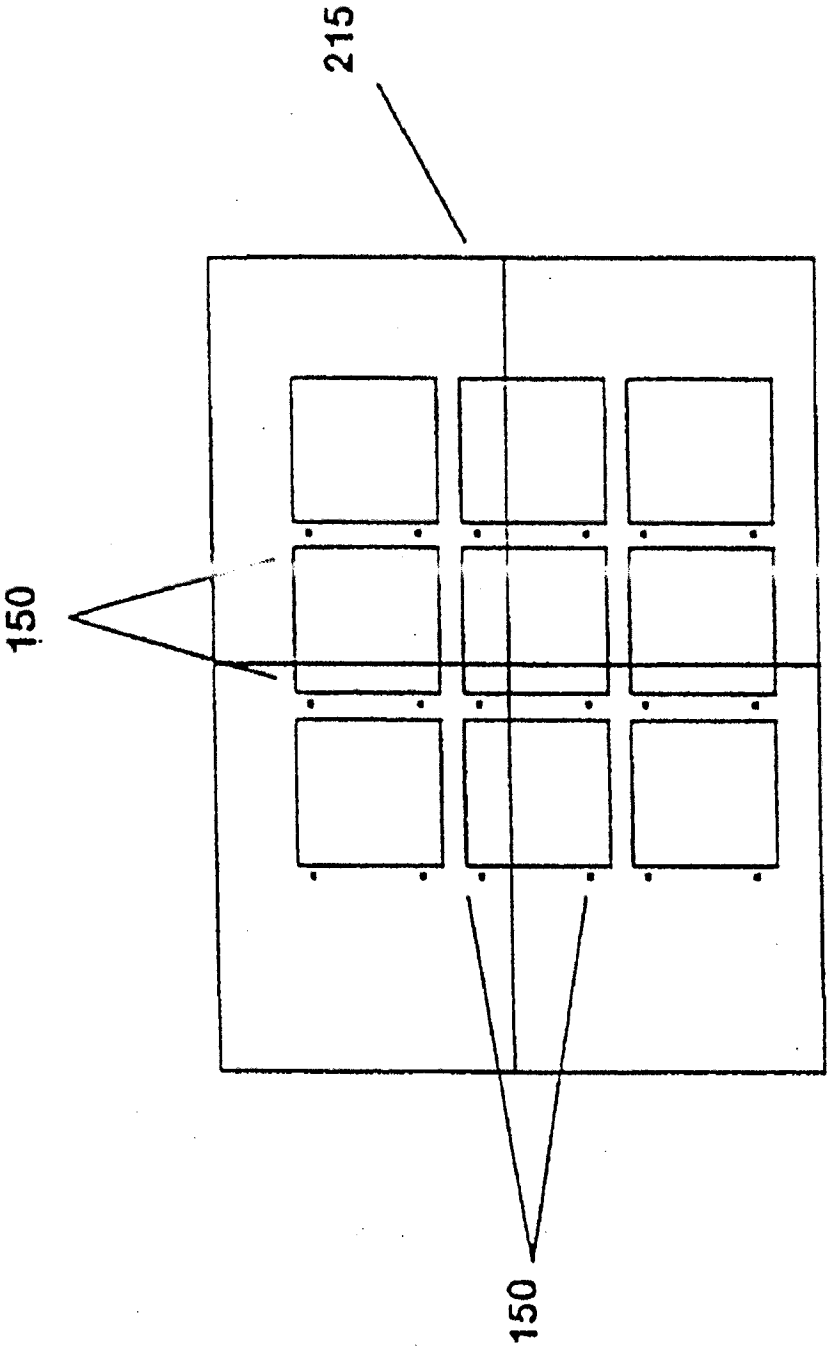


FIG. 2C

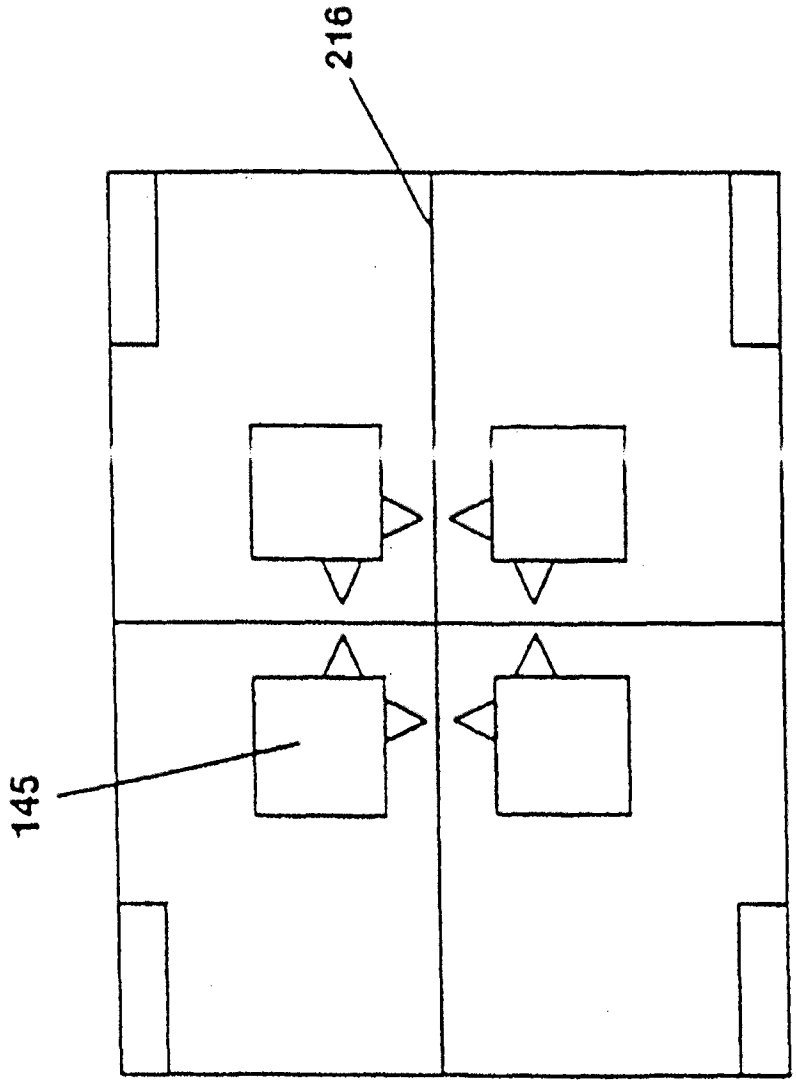
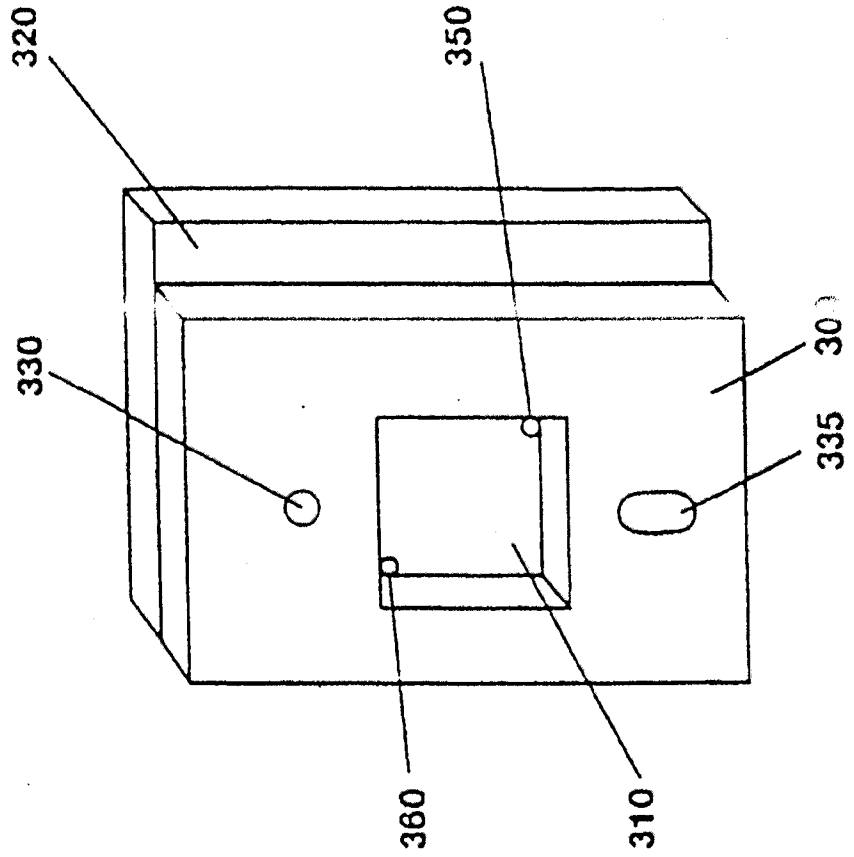


FIG. 2D



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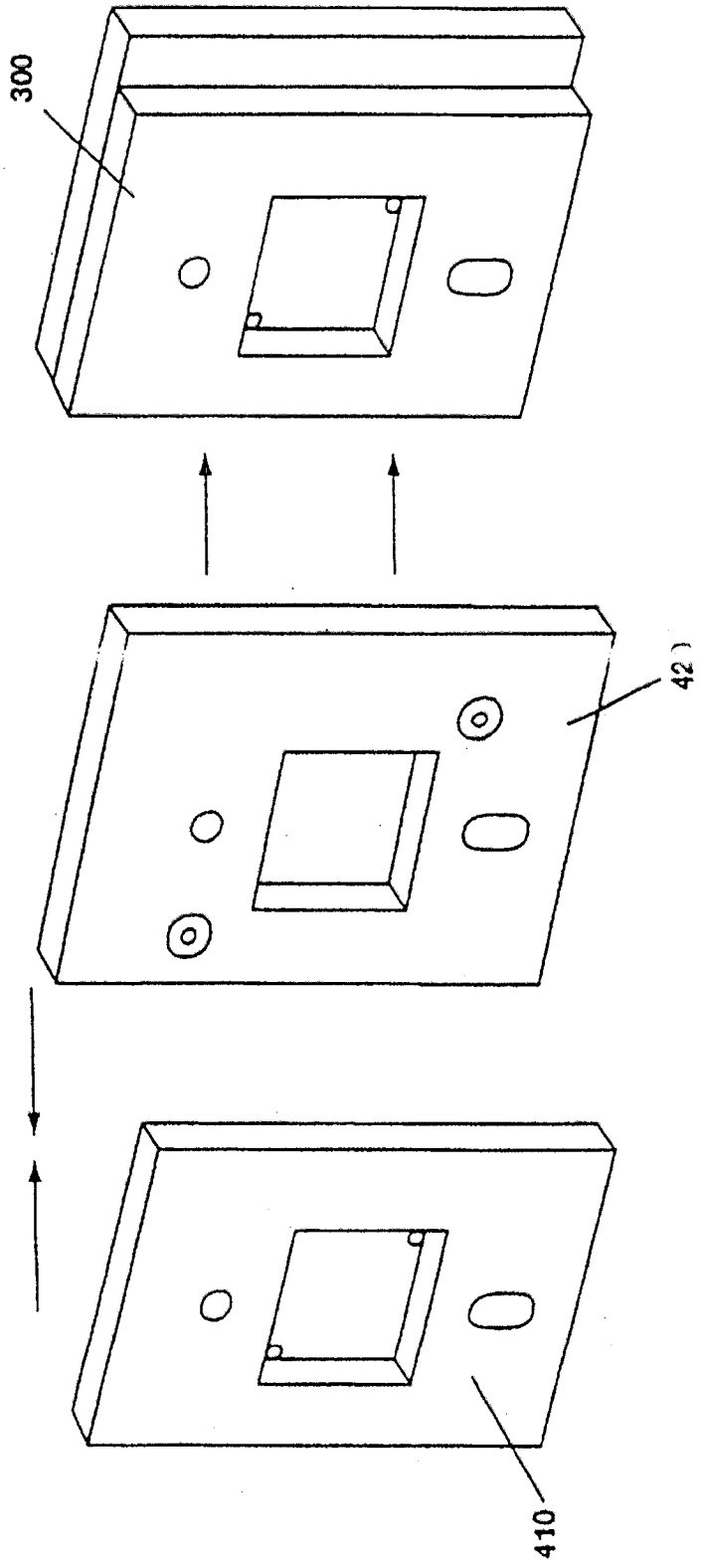
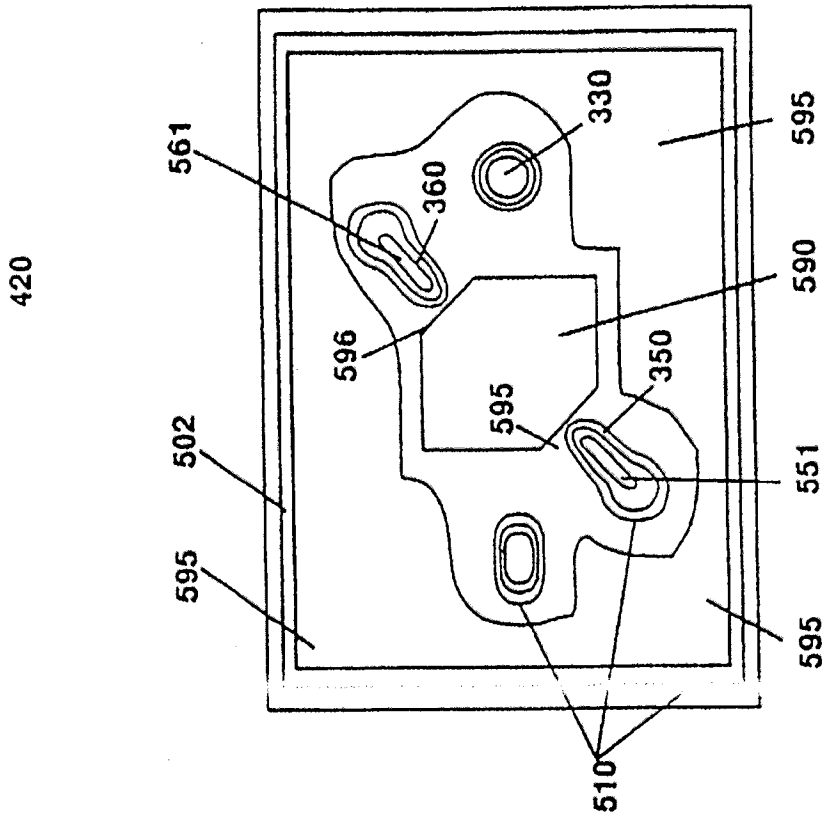


FIG. 4


420
561
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510

FIG. 5B

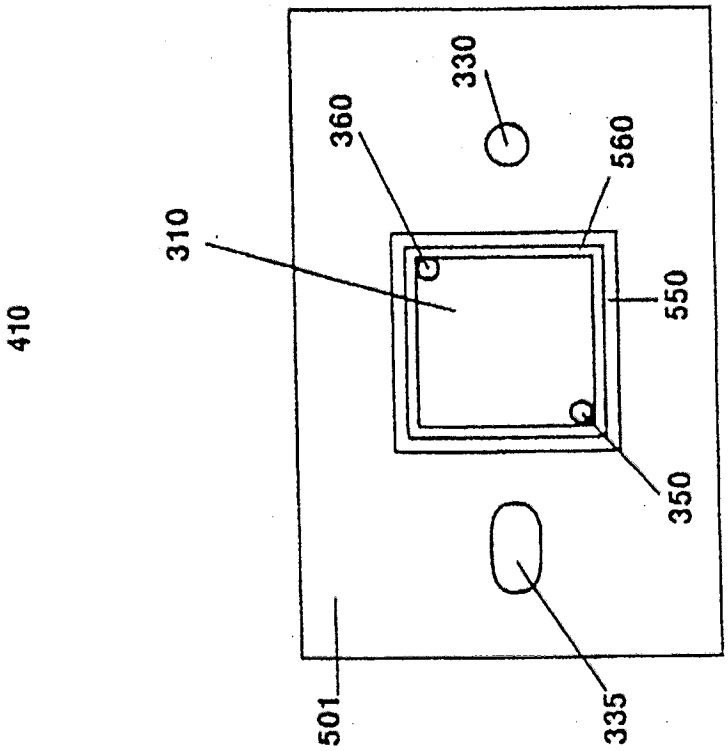
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FIG. 5A

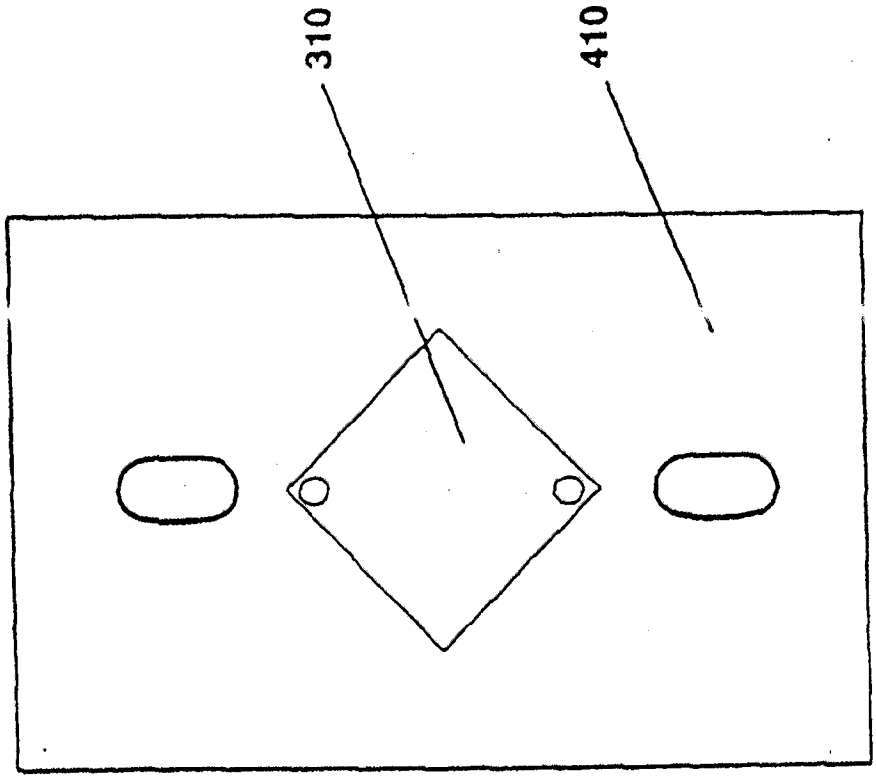

FIG. 5C

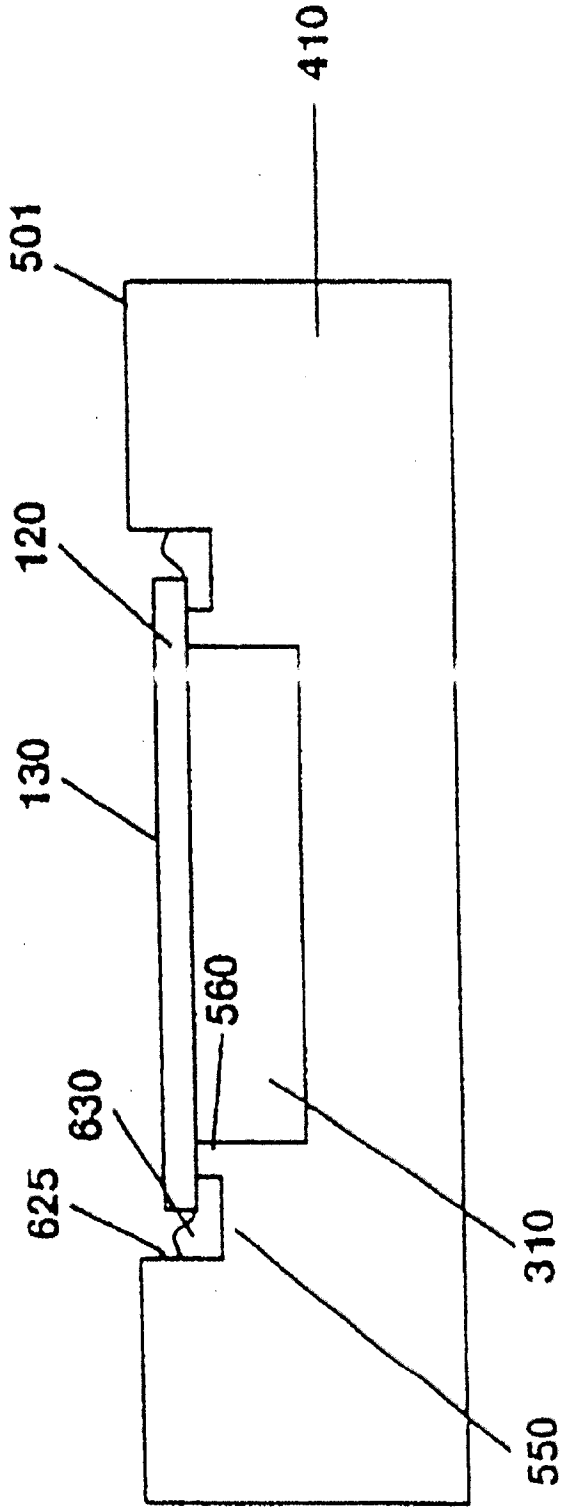

FIG. 6

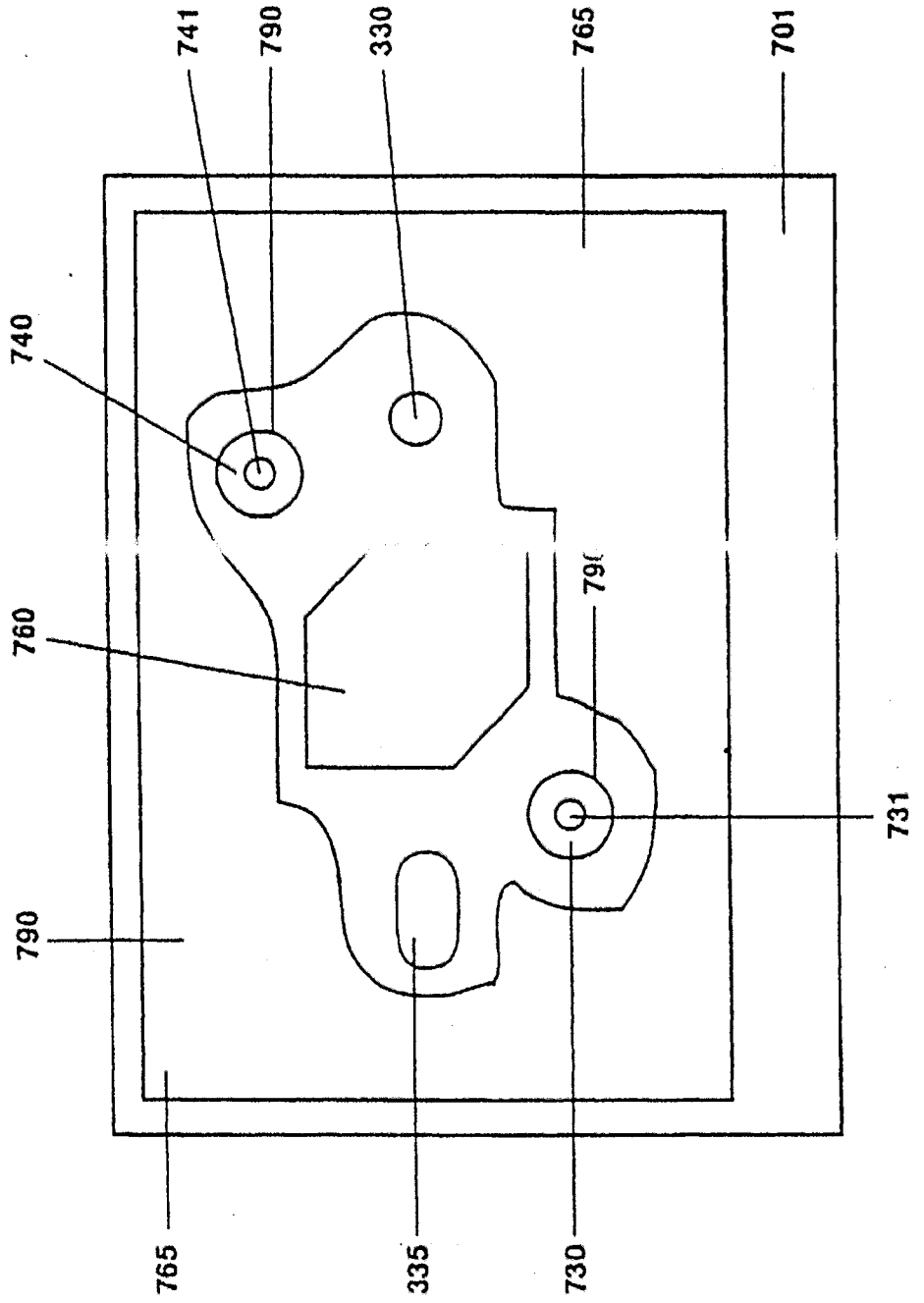

FIG. 7

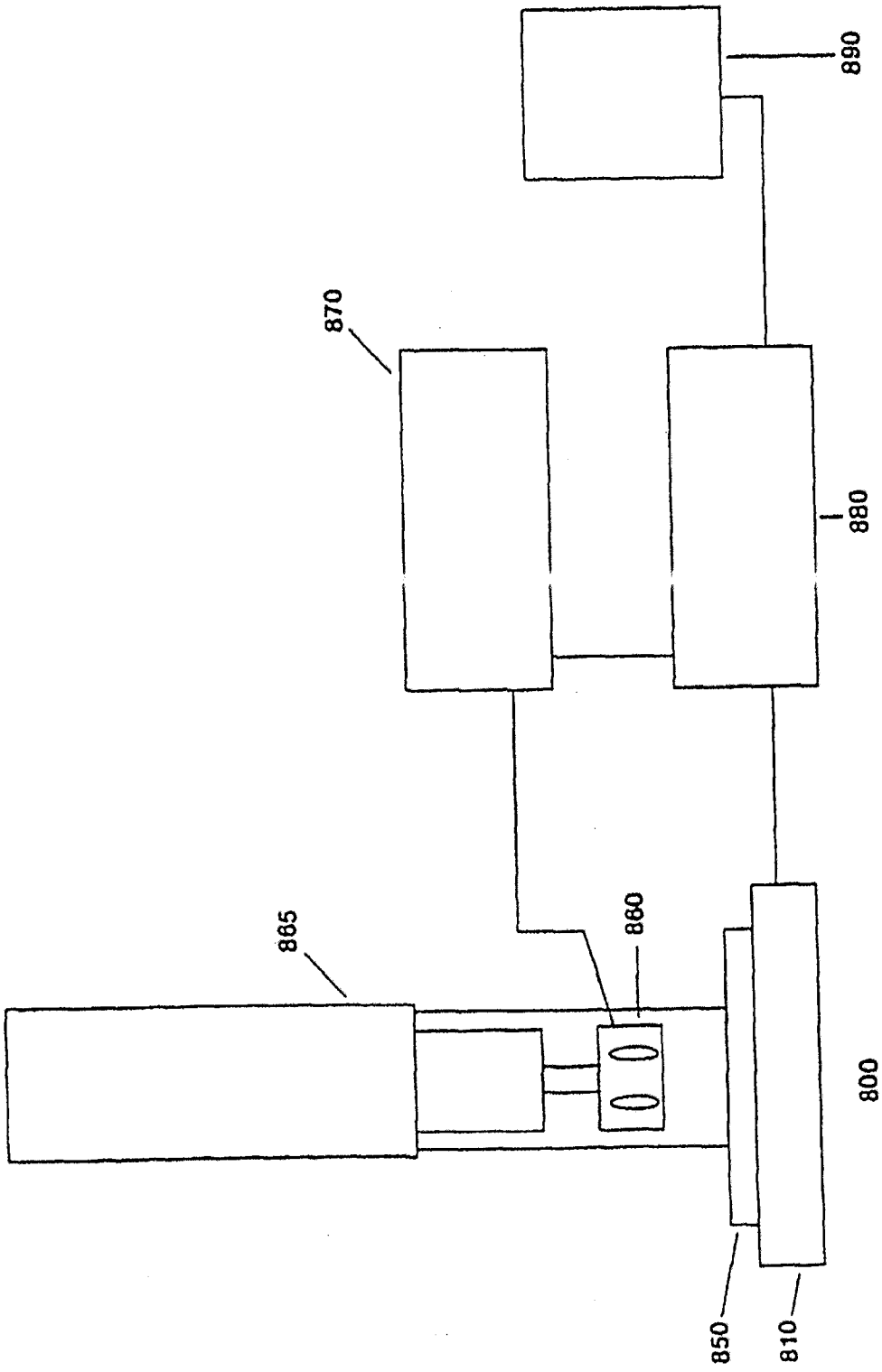

FIG. 8A

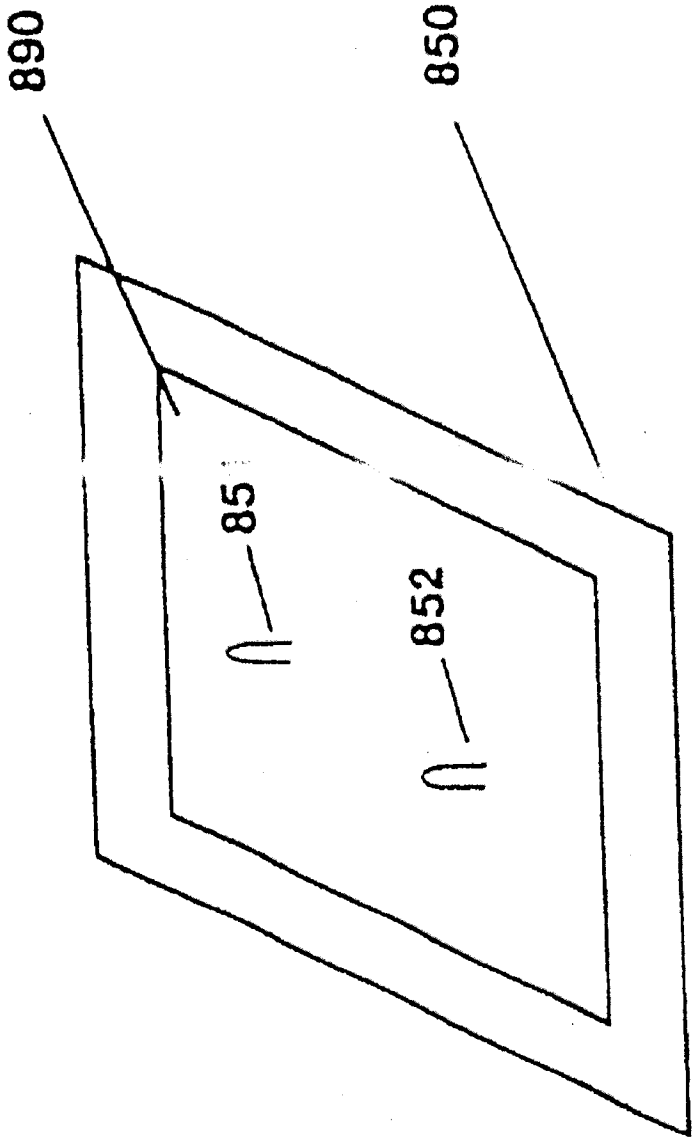

FIG. 8B

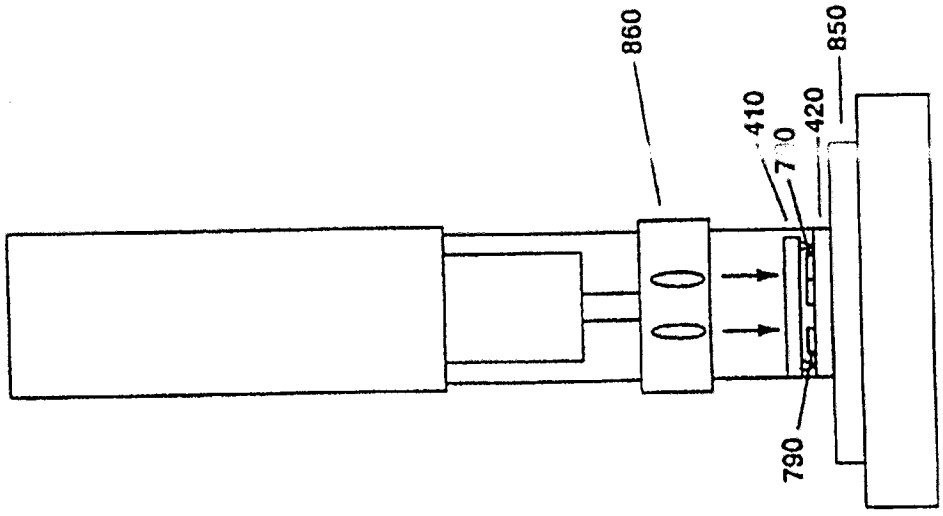

FIG. 9A

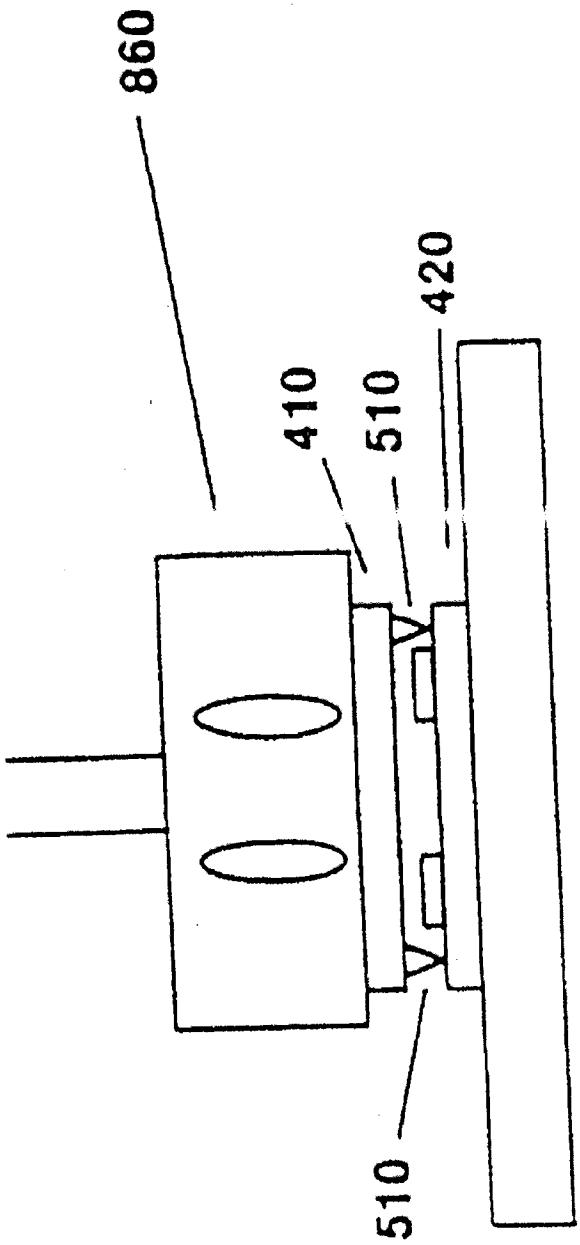

FIG. 9B

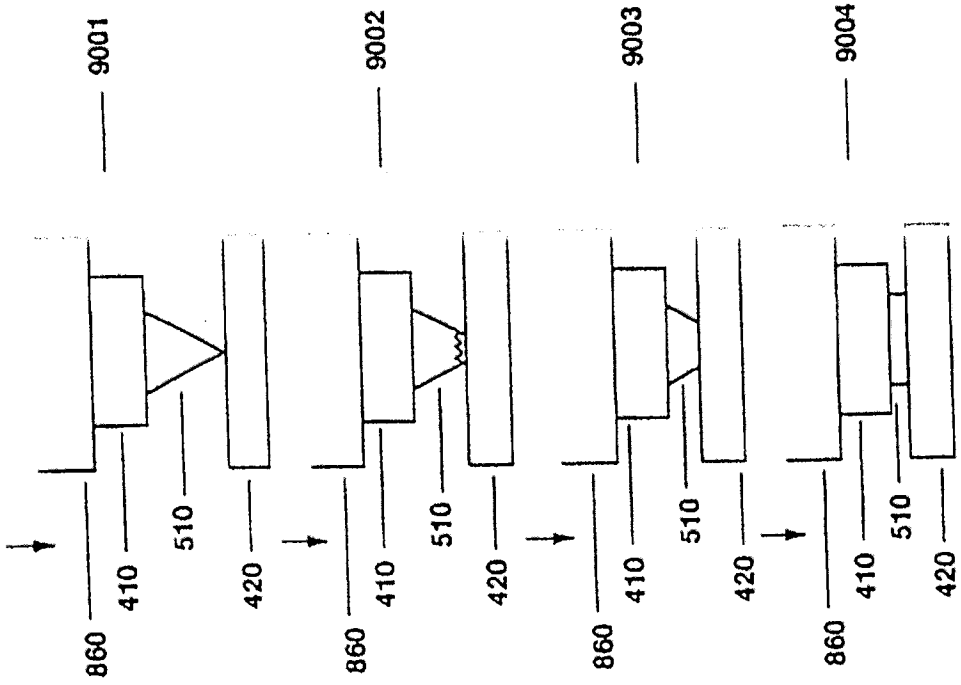

FIG. 9C

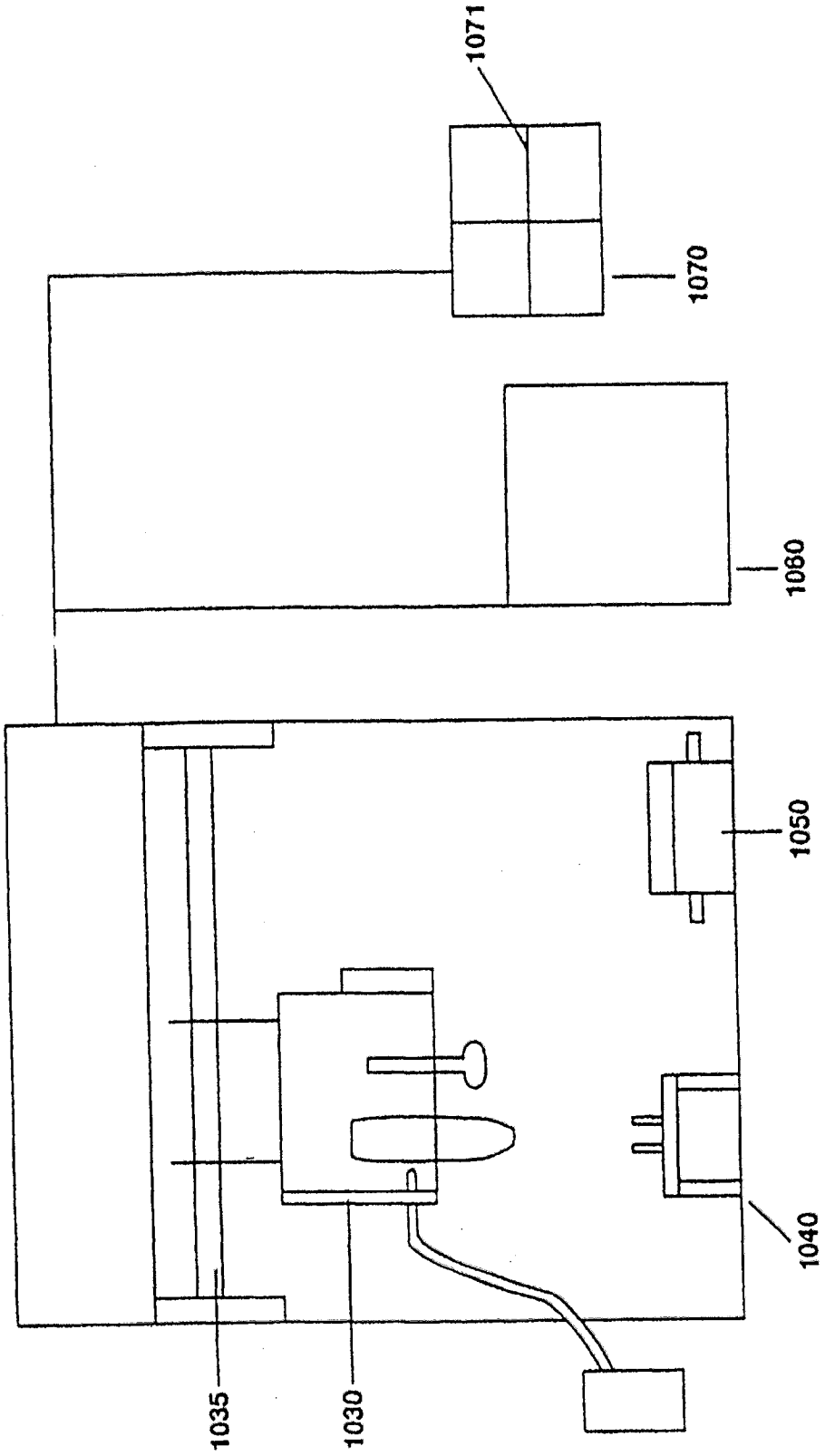

FIG. 10

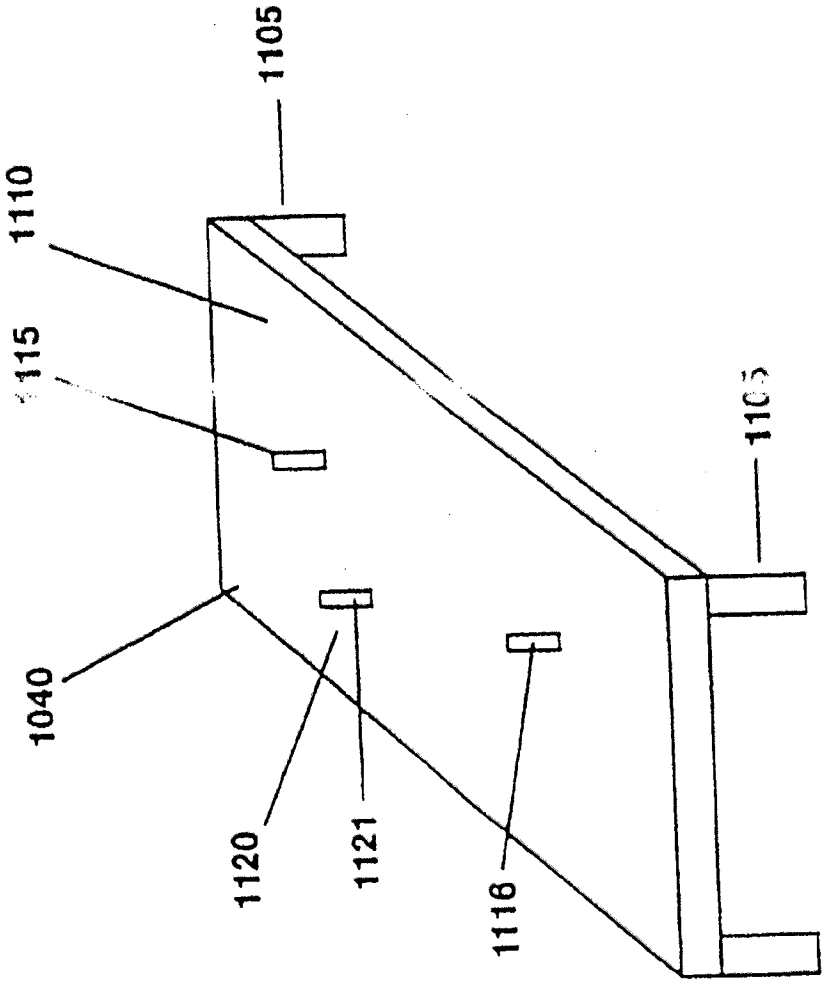

FIG. 11

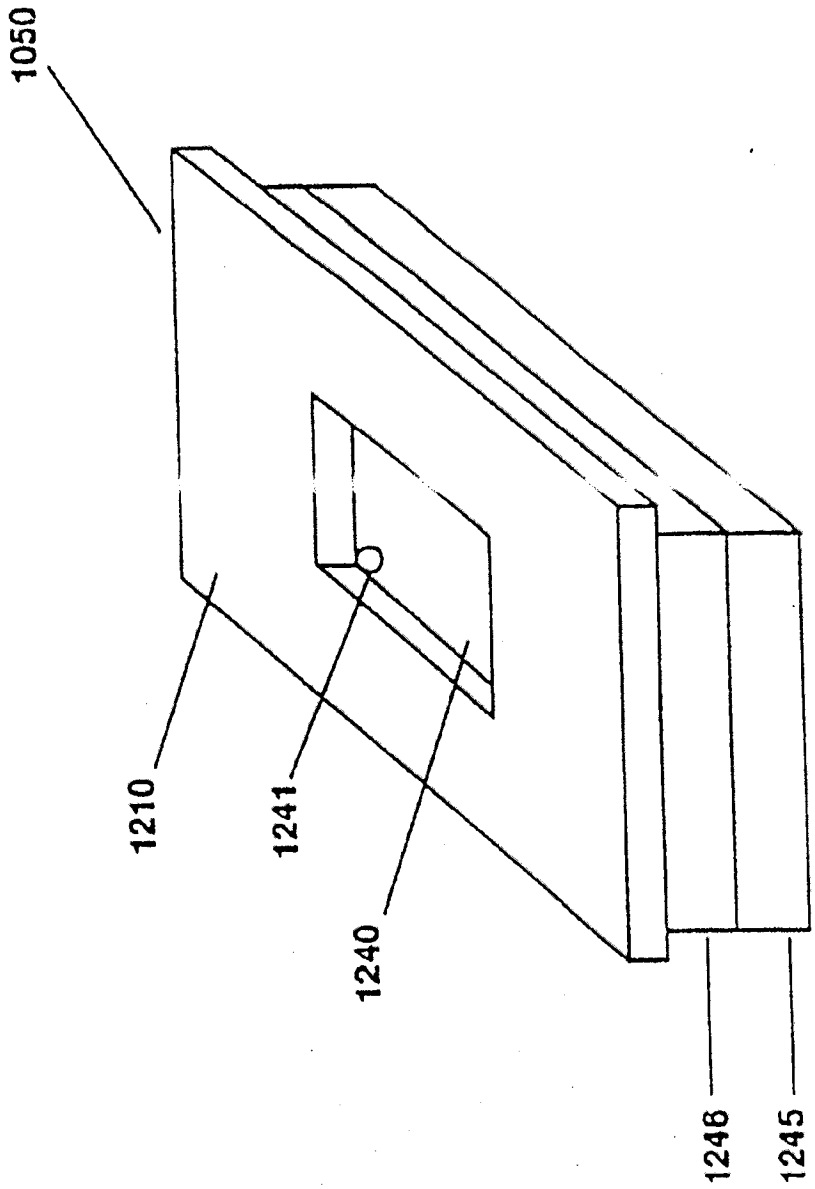

FIG. 12A